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PTO/SB/05 (4/98)
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Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 C.F.R. § 1.53(b))

Attorney Docket No.	ALBIHN W 3.3-258 CONT
First Inventor or Application Identifier	Lennart Cedgård
Title	METHOD FOR THE PRODUCTION OF TABLETS BY PRESSING AND TABLETS PRODUCED BY THE METHOD
Express Mail Label No	EM411073469US

JC712 U.S. PTO
12/17/99

JC712 U.S. PTO
09/465667
12/17/99

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APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

ADDRESS TO: Box Patent Application
Washington, DC 20231

1. [X] * Fee Transmittal Form *(e.g., PTO/SB/17)*
(Submit an original and a duplicate for fee processing)

2. [X] Specification [Total Pages 9]
(preferred arrangement set forth below)
- Descriptive title of the Invention
- Cross References to Related Applications
- Statement Regarding Fed sponsored R & D
- Reference to Microfiche Appendix
- Background of the Invention
- Brief Summary of the Invention
- Brief Description of the Drawings *(if filed)*
- Detailed Description
- Claim(s)
- Abstract of the Disclosure

3. [ ] Drawing(s) *(35 U.S.C. 113)* [Total Sheets]

4. Oath or Declaration [Total Pages 2]
a. [ ] Newly executed (original or copy)
b. [X] Copy from a prior application (37 C.F.R. § 1.63(d))
(for continuation/divisional with Box 16 completed)
i. [ ] DELETION OF INVENTOR(S)
Signed statement attached deleting inventor(s) named in the prior application, see 37 C.F.R. §§ 1.63(d)(2) and 1.33(b).

5. [ ] Microfiche Computer Program *(Appendix)*

6. Nucleotide and/or Amino Acid Sequence Submission *(if applicable, all necessary)*
a. [ ] Computer Readable Copy
b. [ ] Paper Copy (identical to computer copy)
c. [ ] Statement verifying identity of above copies

*** NOTE FOR ITEMS 1 & 13: IN ORDER TO BE ENTITLED TO PAY SMALL ENTITY FEES, A SMALL ENTITY STATEMENT IS REQUIRED (37 C.F.R. § 1.27), EXCEPT IF ONE FILED IN A PRIOR APPLICATION IS RELIED UPON (37 C.F.R. § 1.28).**

ACCOMPANYING APPLICATION PARTS

7. [ ] Assignment Papers (cover sheet & document(s))
8. [ ] 37 C.F.R.§3.73(b) Statement *(when there is an assignee)* [ ] Power of Attorney
9. [ ] English Translation Document *(if applicable)*
10. [ ] Information Disclosure Statement (IDS)/PTO-1449 [ ] Copies of IDS Citations
11. [ ] Preliminary Amendment
12. [X] Return Receipt Postcard (MPEP 503)
(Should be specifically itemized)
13. [ ] * Small Entity Statement(s) *(PTO/SB/09-12)* [ ] Statement filed in prior application, Status still proper and desired
14. [ ] Certified Copy of Priority Document(s)
(if foreign priority is claimed)
15. [X] Other: Three Month Extension Petition

16. If a CONTINUING APPLICATION, *check appropriate box, and supply the requisite information below and in a preliminary amendment:*
[X] Continuation [ ] Divisional [ ] Continuation-in-part (CIP) of prior application No: 09/029336
Prior application information: Examiner Afremova Group / Art Unit: 1651
For CONTINUATION or DIVISIONAL only: The entire disclosure of the prior application, from which an oath or declaration is supplied under Box 4b, is considered a part of the disclosure of the accompanying continuation or divisional application and is hereby incorporated by reference. The incorporation can only be relied upon when a portion has been inadvertently omitted from the submitted application parts.

17. CORRESPONDENCE ADDRESS

[X] *Customer Number or Bar Code Label* 00530 *(Insert Customer No. or Attach bar code label here)* or [ ] *Correspondence address below*

Name	Lerner, David, Littenberg, Krumholz & Mentlik, LLP				
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Name (Print/Type)	Arnold H. Krumholz	Registration No. (Attorney/Agent)	25,428
Signature		Date	12/17/99

Burden Hour Statement. This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Box Patent Application, Washington, DC 20231.

TITLE: Method for the production of tablets by pressing and tablets produced by the method.

TECHNICAL FIELD:

The present invention relates to a method for the production of tablets by pressing of tablet material which contains microorganisms.

PRIOR ART:

Tablets are usually produced by pressing of a pulverulent tablet mass in a suitable shape in a so-called tablet punching machine. The tablets may have different shape and be of different size and they may also be of different hardness dependent on the properties of the tablet mass and the pressure to which they are subjected during the punching of the tablets.

When the tablets are formed heat is developed as a result of the friction against the mould surfaces and the inner friction in the tablet mass. Since the tablets usually consist of chemicals and the temperature increase is not too high, this will not create any problem since the chemicals can resist this heat increase and also are cooled rapidly. However, some tablet masses contain living microorganisms, such as bacteria, which are sensitive to high temperatures and because of this some of these bacteria die during the tablet punching.

TECHNICAL PROBLEM:

Tablets which contain microorganisms, for instance in the form of bacteria, and which are intended to contain such organisms will lose a part of or all of their value when the microorganisms are destroyed during the tablet punching. This cannot be avoided by simply using a lower pressure on the conventional tablet mass and thereby creating a lower heat development since the tablet must be

subjected to a certain pressure so that it maintains its shape and is not crumbled. For known tablet masses it is not unusual that a reduction of the viability (survival) of the bacteria in the tablet is up to 80% and even more.

SOLUTION:

It has therefore always been a problem to be able to produce tablets which contain microorganisms in the form of bacteria with a lesser reduction of the viability from tablet mass to a complete tablet and therefore according to the invention a method has been obtained for the production of tablets by pressing of tablet material comprising living organisms, which is characterized in that the tablet material also contains oligosaccharides consisting of more than two monosaccharides.

According to the invention, it is suitable that the oligosaccharides consist of fructose oligosaccharides, preferably inulin.

According to the invention it is suitable that the oligosaccharides are present in an amount of 40-99.5 % by weight of the tablet material.

The tablet material according to the invention can suitably contain microorganisms consisting of lactic acid producing bacteria.

The invention also comprises tablets produced by the method according to the invention, which tablets contain oligosaccharides and microorganisms whereby the oligosaccharides suitably consist of fructose oligosaccharides, preferably inulin.

The tablets according to the invention may contain lactic acid producing bacteria as microorganisms and they may also

contain other additives such as polysaccharides, for example microcrystalline cellulose and starch, as well as other additives such as calcium diphosphate.

DETAILED DESCRIPTION:

The tablets according to the invention comprise microorganisms, preferably lactic acid producing bacteria cultures known as probiotica, which are intended to normalise or balance bacterial flora being present in the stomach and the intestine of humans or animals, but they may also contain other types of bacteria.

By mixing oligosaccharides, preferably fructose oligosaccharides, in the tablet mass as a so-called supporting substance the tablet punching is facilitated, which makes it possible to punch tablets at a lower pressure and lower heat development at the same time as the hardness of the tablet is maintained. The brittleness of the tablet, the friability, is surprisingly not changed with the tablet mass according to the present invention.

Due to this new composition, the punching pressure for the tablet making maybe reduced by up to 50% compared to conventional tablet punching methods without any reduction of the friability. This friability according to the invention will be 0.3-0.5, which is to be compared with the reference values which are accepted according to GMP (Good Manufacturing Practice) which are within the range of 0.1-1.0. The friability is expressed in percent weight reduction of the tablets when they are rotated 100 revolutions in a standard testing machine.

The amount of oligosaccharides depends on different crystalline qualities but may suitably be 99.5-40 weight percent of the total tablet mass without admixing any other supporting substance. However, if desired, known supporting

substances such as calcium diphosphate, microcrystalline cellulose and starch may be added in a suitable small amount. A smaller addition of oligosaccharides can, however, give rise to a smaller difference with regard to the viability compared with tablet masses containing only conventional supporting substances.

The tablets according to the present invention have a lower hardness due to the lower punching pressure when the tablets are formed but an increased viability for the strain of bacteria, which makes every tablet more efficient than conventional tablets. By not pressing the tablets so hard the yield of tablets for a given amount of tablet mass will also increase.

The invention will be described more in detail below by means of two examples, of which Example 1 describes a method according to the present invention and Example 2 describes a method of conventional kind.

Example 1: recipe having an active substance and tablet filling material

Str. thermophilus & L. bulgaricus	50%
Bifidobacterium animalis	0.5%
L. plantaris	0.5%
Inulin (fructose oligosaccharides)	49%
	100%

Hardness: 2.75 kp Friability: 0.3
Viability original granulate: 5E8 cfu/g
Viability tablet: 3E8 cfu/g
40% reduction of cfu (colony forming units)

Example 2: recipe having active substance and tablet filling material

Str. thermophilus & L. bulgaricus	50%
Bifidobacterium animalis	0.5%
L. plantaris	0.5%
Calcium diphosphate	20%
Microcrystalline cellulose	18%
Starch	11%
	100%

Hardness: 5.5 kp Friability: 0.3%
Viability original granulate: 5E8 cfu/g
Viability tablet: 1E8 cfu/g
80% reduction of cfu (colony forming units)

As appears from the above examples, the friability is maintained unchanged with a value of 0.3 whereas the hardness has been decreased to 2.75 kp compared with 5.5 kp for the conventional method. The viability has increased from 1E8 cfu/g to 3E8 cfu/g according to the invention. The reduction of cfu from tablet mass to tablet during the tablet punching became only 40% according to the new method and 80% according to the conventional method.

Accordingly, the new method results in an increased maintained viability after tablet punching of up to 200% compared with conventional tablet fillers. The increased yield results in an appreciably better economy and quality improvement of the above products.

The invention is not limited to the embodiments shown above but can be varied in different ways within the scope of the claims.

CLAIMS:

1. Method for the production of tablets having high viability in the tablet by pressing tablet material containing living microorganisms, characterized in that the tablet material also contains oligosaccharides.

2. Method according to claim 1 characterized in that the oligosaccharides are present in an amount of 40-99.5 percent by weight of the tablet material.

3. Method according to any of claims 1-2, characterized in that the oligosaccharides consist of fructose oligosaccharides.

4. Method according to any of claims 1-3, characterized in that the oligosaccharides consist of inulin.

5. Method according to any of claims 1-4, characterized in that the microorganisms consist of lactic acid producing bacteria.

6. Tablets produced according to any of claims 1-5 containing oligosaccharides and microorganisms.

7. Tablets according to claim 6, characterized in that the oligosaccharides consist of fructose oligosaccharides.

8. Tablets according to any of claims 6-7, characterized in that the oligosaccharides consist of inulin.

9. Tablets according to any of claims 6-8, characterized in that the microorganisms consist of lactic acid producing bacteria.

10. Tablets according to any of claims 6-9, characterized in that they also contain polysaccharides such as microcrystalline cellulose and starch as well as other additives such as calcium diphosphate.

AMENDED CLAIMS

[received by the International Bureau on 24 December 1996 (24.12.96); original claims 1 - 10 replaced by amended claims 1 - 10 (2 pages)]

1. Method for the production of tablets having high viability in the tablet by pressing tablet material containing living microorganisms, c h a r a c t e r i z e d i n that the tablet material also contains oligosaccharides consisting of more than two monosaccharides.

2. Method according to claim 1 c h a r a c t e r i z e d i n that the oligosaccharides are present in an amount of 40-99.5 percent by weight of the tablet material.

3. Method according to any of claims 1-2, c h a r a c t e r i z e d i n that the oligosaccharides consist of fructose oligosaccharides.

4. Method according to any of claims 1-3, c h a r a c t e r i z e d i n that the oligosaccharides consist of inulin.

5. Method according to any of claims 1-4, c h a r a c t e r i z e d i n that the microorganisms consist of lactic acid producing bacteria.

6. Tablets produced according to any of claims 1-5 containing oligosaccharides and microorganisms.

7. Tablets according to claim 6, c h a r a c t e r i z e d i n that the oligosaccharides consist of fructose oligosaccharides.

8. Tablets according to any of claims 6-7, c h a r a c t e r i z e d i n that the oligosaccharides consist of inulin.

9. Tablets according to any of claims 6-8, characterized in that the microorganisms consist of lactic acid producing bacteria.

10. Tablets according to any of claims 6-9, characterized in that they also contain polysaccharides such as microcrystalline cellulose and starch as well as other additives such as calcium diphosphate.

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

ATTORNEY'S DOCKET NO.: ALBIHN W 3.3-258

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name;

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: "Method for the production of tablets by pressing and tablets produced by the method", the specification of which

☐ is attached hereto

☒ was filed on 23.08.96 as United States Application Number or PCT International Application Number PCT/SE96/01043 and was amended on 24.12.96 (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate, or any PCT international application having a filing date before that of the application on which priority is claimed:

PRIOR FOREIGN APPLICATION(S)			
COUNTRY	APPLICATION NUMBER	DATE OF FILING (month, day, year)	PRIORITY CLAIMED
Sweden	9502941-9	08-25-95	YES ☒ NO ☐
			YES ☐ NO ☐
			YES ☐ NO ☐
LISTING OF FOREIGN APPLICATIONS CONTINUED ON PAGE 3 HEREOF ☐ YES ☒ NO			

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below:

Application Number: _____ Filing Date: _____

Application Number: _____ Filing Date: _____

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s), or § 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

U.S. Parent Application Serial Number: _____ Parent Filing Date: _____ Parent Patent No.: _____

U.S. Parent Application Serial Number: _____ Parent Filing Date: _____ Parent Patent No.: _____

PCT Parent Number: _____ Parent Filing Date: _____

LISTING OF US APPLICATIONS CONTINUED ON PAGE 3 HEREOF: ☐ YES ☒ NO

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.

Lawrence I. Lerner, Reg No 19,516, Sidney David Reg No 22,768, Joseph S Littenberg, Reg No 20,832, Arnold H Krumholz, Reg No 25,428, William L Mentlik, Reg No 27,108, John R Nelson, Reg. No. 26,573, Roy H Wepner, Reg No 28,350, Stephen B Goldman, Reg No 28,512, Paul H Kochanski, Reg No 29,660, Marcus J Millet, Reg No. 28,241, Bruce H Sales, Reg No. 32,793; Daniel H. Bobis, Reg No 16,694, Peter J Butch III, Reg. No 32,203, Keith E Gilman, Reg No. 32,137, Robert B. Cohen, Reg No 32,768, Arnold B Dompieri, Reg No 29,736, Michael H. Teschner, Reg No. 32,862, Jeffrey S Dickey, Reg No. 35,858, Gregory S Gewirtz, Reg No 36,522, Jonathan A. David, Reg No 36,494, Shawn P. Foley, Reg No. 33,071, Robert T Canavan, Reg. No. 37,592

SEND CORRESPONDENCE TO:	DIRECT TELEPHONE CALLS TO:
LERNER, DAVID, LITTENBERG, KRUMHOLZ & MENTLIK 600 South Avenue West Westfield, New Jersey 07090	*(name and telephone number)* Arnold H. Krumholz (908) 654-5000 Fax: (908) 654-7866

DECLARATION – Page 2

ATTORNEY DOCKET NO. ALBIHN W 3.3-258

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor (given name, family name): Lennart Cedgård

Inventor's signature _____ **Date** February 16, 1998

Residence: Göteborg, Sweden Citizenship: Sweden

Post Office Address: Skolgatan 26, S-413 02 Göteborg, Sweden

Full name of second joint inventor, if any (given name, family name): _____

Second Inventor's signature _____ **Date** _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of third joint inventor, if any (given name, family name): _____

Third Inventor's signature _____ **Date** _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of fourth joint inventor, if any (given name, family name): _____

Fourth Inventor's signature _____ **Date** _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of fifth joint inventor (given name, family name): _____

Fifth Inventor's signature _____ **Date** _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of sixth joint inventor, if any (given name, family name): _____

Sixth Inventor's signature _____ **Date** _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of seventh joint inventor, if any (given name, family name): _____

Seventh Inventor's signature _____ **Date** _____

Residence: _____ Citizenship: _____

Post Office Address: _____

Full name of eighth joint inventor, if any (given name, family name): _____

Eighth Inventor's signature _____ **Date** _____

Residence: _____ Citizenship: _____

Post Office Address: _____

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GP 1651

PATENT
ALBIHN W 3.3-258 CONT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of Lennart Cedgård	:	
	:	Group Art Unit: 1651
A Continuation of U.S. Application No. 09/029,336	:	
	:	Examiner: V. Afremova
Filing Date: Herewith	:	
For: METHOD FOR THE PRODUCTION OF TABLETS BY PRESSING AND TABLETS PRODUCED BY THE METHOD	:	Date: December 17, 1999

X

Assistant Commissioner for Patents
Washington, D.C. 20231

EXTENSION PETITION

Sir:

The undersigned attorney respectfully petitions for a three-month extension of time to reset the deadline for response to the Office Action in the above-identified application from September 17, 1999 to and including December 17, 1999. Applicant's Continuing Application is enclosed herewith.

Please charge Deposit Account No. 12-1095 in the amount of $870.00.

In the event the actual fee is greater than the amount above, the Patent Office is authorized to charge any deficiency to our Deposit Account No. 12-1095.

Respectfully submitted,

LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK, LLP

ARNOLD H. KRUMHOLZ
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EXPRESS MAIL LABEL NUMBER: EM411073469US